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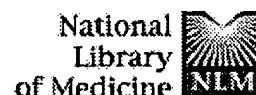
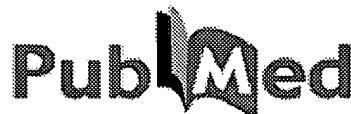
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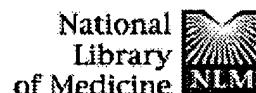
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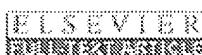
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**Immunoregulatory role of H-2 and intra-H-2 alleles on antibody responses to recombinant preparations of B-subunits of Escherichia coli heat-labile enterotoxin (rEtxB) and cholera toxin (rCtxB).**

Nashar TO, Hirst TR.

Research School of Biosciences, University of Kent at Canterbury, UK.

The immunoregulatory role of H-2 and intra-H-2 alleles on antibody responses to recombinant preparations of B-subunits of Escherichia coli heat-labile enterotoxin (rEtxB) and cholera toxin (rCtxB) is reported. Oral delivery of rEtxB to congenic mice of several different H-2 haplotypes resulted in H-2 dependent serum IgG responses (H-2d > H-2b = H-2q > H-2a > H-2k) and a similar spectrum of intestinal IgA responses in those strains tested. Responses to rEtxB and rCtxB were found to be differentially modulated by the H-2 locus, with significant differential effects in H-2b and H-2d congenic strains (H-2d > H-2b for rEtxB; H-2b > H-2d for rCtxB). Additionally, it was found that when rEtxB was fed to mice previously primed (orally) with either rEtxB or rCtxB only those mice primed with rEtxB exhibited a booster response. A second booster immunisation with rEtxB in rCtxB-primed mice produced an H-2 dependent spectrum of responses characteristic of those elicited by rEtxB, with the antibodies predominantly directed against rEtxB and not rCtxB. These results indicate that the differential response to rEtxB and rCtxB is set at the T- and B-cell level. Also, immunoregulation of antibody responses to rEtxB by intra-H-2 I-E in mice transgenic for the entire IEka gene was investigated. No significant difference between responses in transgene-positive and -negative mice was found, suggesting that antigen presentation does not involve I-E, but occurs in the context of I-A. (ABSTRACT TRUNCATED AT 250 WORDS)

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## Protective Mucosal Immunity to Ocular Herpes Simplex Virus Type 1 Infection in Mice by Using *Escherichia coli* Heat-Labile Enterotoxin B Subunit as an Adjuvant

C. M. Richards,\* A. T. Aman, T. R. Hirst, T. J. Hill, and N. A. Williams

Department of Pathology and Microbiology, School of Medical Sciences, University of Bristol, Bristol BS8 1TD, United Kingdom

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The potential of nontoxic recombinant B subunits of cholera toxin (rCtxB) and its close relative *Escherichia coli* heat-labile enterotoxin (rEtxB) to act as mucosal adjuvants for intranasal immunization with herpes simplex virus type 1 (HSV-1) glycoproteins was assessed. Doses of 10 µg of rEtxB or above with 10 µg of HSV-1 glycoproteins elicited high serum and mucosal anti-HSV-1 titers comparable with that obtained using CtxB (10 µg) with a trace (0.5 µg) of whole toxin (Ctx-CtxB). By contrast, doses of rCtxB up to 100 µg elicited only meager anti-HSV-1 responses. As for Ctx-CtxB, rEtxB resulted in a Th2-biased immune response with high immunoglobulin G1 (IgG1)/IgG2a antibody ratios and production of interleukin 4 (IL-4) and IL-10 as well as gamma interferon by proliferating T cells. The protective efficacy of the immune response induced using rEtxB as an adjuvant was assessed following ocular challenge of immunized and mock-immunized mice. Epithelial disease was observed in both groups, but the immunized mice recovered by day 6 whereas mock-immunized mice developed more severe corneal disease leading to stromal keratitis. In addition, a significant reduction in the incidence of lid disease and zosteriform spread was observed in immunized animals and there was no encephalitis compared with 95% encephalitis in mock-immunized mice. The potential of such mucosal adjuvants for use in human vaccines against pathogens such as HSV-1 is discussed.

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\* Corresponding author. Mailing address: Department of Pathology and Microbiology, School of Medical Sciences, University of Bristol, University Walk, Bristol BS8 1TD, United Kingdom. Phone: 44 (0)117 928 7585. Fax: 44 (0)117 928 7896. E-mail: [Claire.M.Richards@bristol.ac.uk](mailto:Claire.M.Richards@bristol.ac.uk).

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